

Yale Tobacco Center of Regulatory Science

Menthol's Effects on the Nicotine Reinforcement in Smokers (Project 2)

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Abstract:

Epidemiological studies suggest that menthol is a potential contributor to the development and maintenance of tobacco addiction. Menthol may have a special role in tobacco addiction given that nicotine, compared to other drugs of abuse, is a relatively weak reinforcer and other reinforcers combined with nicotine may facilitate development and maintenance of addiction. The potential reinforcing properties of menthol have not been examined with systematic studies in controlled settings. One roadblock in determining the contribution of menthol to cigarette reinforcement has been the brand loyalty of smokers. Thus, novel approaches are needed that will minimize the conditioned association between nicotine and menthol. The overall goal of this project is to examine the reinforcing effects of menthol in combination with nicotine. We will examine if acute menthol administration by either e-cigarette (Study 1) or sublingual tablet (Study 2), compared to control flavors, will change the reinforcing effects of pure nicotine administered intravenously. We are proposing two double-blind, placebo-controlled studies each enrolling 30 menthol and 30 non-menthol cigarette smokers matched for race, gender, and level of nicotine intake. Both studies will use a crossover design such that each smoker will be tested under low or high dose of menthol or non-menthol flavors. Menthol will be administered concurrently with nicotine (saline, 5 µg/kg and 10 µg/kg). Use of both inhaled and sublingual routes for menthol administration will provide complementary information for the possible mechanism by which menthol may change nicotine reinforcement. E-cigarette delivery provides sensory effects in the throat and upper airways like those experienced with inhaled tobacco products, and the sublingual route will produce local sensory effects in the mouth and throat, consistent with menthol exposure in oral tobacco products. The intravenous nicotine administration produces rapid nicotine delivery and reinforcing effects in smokers. This proposal is highly significant because it may be an important step in determining the reinforcing effects of menthol, alone or in combination with nicotine. The results of this study will contribute to the knowledge needed to develop science-based policies regarding menthol as an additive in cigarettes.